REMARKS

I. Amendments

Applicants are appreciative of the favorable indication that claims 3-14 and 21-26 are directed to patentable subject matter. Applicants submit that the remaining claims 1, 2, 15-20, 27-29, 32, 35, 36, and 38 are also directed to patentable subject matter in view of the amendments and arguments presented herein.

II. Rejections under 35 U.S.C. §112

A. 35 U.S.C. §112, second paragraph

Claims 18-20 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleges that the terms "higher temperature", "lower temperature", and "preparation", as recited in claims 18-20, are confusing. Applicants have amended claims 18-23 by substituting the objected term with the replacement expression as shown in the table below. Support for the replacement temperature expression, i.e., higher/lower temperature, is provided by original claims 25 and 26, respectively, now canceled.

Original term in claims 18-23	Replacement expression
higher temperature	temperature of 40°C or greater
lower temperature	temperature lower than 40°C
preparation	obtaining

On page 2 of the Office Action, the Examiner questions how claims 18-20 differ from routine purification steps. Applicants reply that the term "purification" is understood in the relevant art to refer to the conversion of a substance into a purer, less polluted product. In contrast, claims 18-20 are directed to the conversion of an amorphous substance into one or more crystalline forms. Accordingly, these claims are directed to processes for obtaining particular crystalline forms of the recited mesylate salt, rather than to the reduction of impurities in the salt. Therefore, for the sake of clarity, the expression "preparation" has been deleted from claims 18-23 and substituted with --obtaining--. Support is provided throughout the original

specification. Claims 27 and 38 have been amended to delete dependencies upon cancelled claims 25 and 26.

B. 35 U.S.C. §112, first paragraph

Claims 29, 31, 32, 35, 36, and 38 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

Claim 29 has been amended to recite a method for inhibiting gastric acid secretion. Claim 31 has been cancelled. Claim 32 has been re-written as an independent claim directed to the treatment of the expressly recited gastrointestinal disorders. Applicants believe that product-by-process claim 38 was mistakenly grouped with this rejection of the method of treatment claims.

A determination of enablement cannot be made in a vacuum. Rather, as noted by the Examiner at pages 3-5 of the Office Action, the Wands factors such as (a) the nature of the invention, (b) the state of the prior art, and (c) the relative skill of those in the art must be taken into consideration.

The prior art is replete with enabling disclosures directed to the administration and efficacy of the class of imidazopyradine compounds to which the claimed invention belongs for the treatment and/or inhibition of gastric-acid secretion, gastric-acid related diseases, and airway disorders. In addition to the prior art cited and discussed in the specification, the Examiner's attention is directed to the prior art cited by the Examiner in support of the obviousness rejections of record: WO 2003/094967 (treatment of airway disorders); WO 2002/064118 (treatment of gastric acid related disorders); and WO 1999/055706 (inhibition of gastric acid secretion).

For example, Applicants submit that the "high[ly]" skilled artisan, as noted by the Examiner on page 5 of the Office Action, would recognize that the instant compounds can be used for inhibiting gastric acid secretion. As disclosed in the specification at page 2, international patent publications WO 99/55705 and WO 99/55706 disclose a number of imidazopyridine derivatives which are potassium-competitive blockers of acid secretion. WO 99/55706 specifically discloses the synthesis of the neutral form of 2,3-dimethyl-8-(2,6-dimethylbenzylamino)-N-hydroxyethyl-imidazo-[1,2-a]pyridine-6-carboxamide at Example 1.3,

page 23. This publication also provides *in vitro* biological test information at page 52 discussing acid secretion inhibition in isolated rabbit gastric glands. At pages 52-55, the publication provides *in vivo* test information regarding the inhibiting effect of the test compounds on acid secretion in female rats; the bioavailablity of the compounds in rats; and the inhibition of gastric acid secretion and bioavailability in conscious dogs.

Consequently, the ordinary practitioner would recognize that 2,3-dimethyl-8-(2,6-dimethylbenzylamino)-N-hydroxyethyl-imidazo-[1,2-a]pyridine-6-carboxamide, as well as the claimed derivative mesylate salts, would be useful in the treatment and/or inhibiting of gastric-acid secretion, gastric-acid related diseases and airway disorders. Based on (a) the nature of the invention, (b) the state of the prior art, and (c) the relative skill of those in the art must be taken into consideration, the level of predictability is high that the claimed substituted imidazo-[1,2-a]pyridine compounds will have the expected pharmacological and therapeutic effect.

In addition to the guidance provided by the prior art, typical daily dosages of the claimed compounds are discussed in the specification at page 15, lines 10-18, and dosage forms comprising the compounds are described at page 15, lines 10-page 18, line 4. Therefore, the skilled artisan has sufficient guidance to practice the claimed methods of treatment for the inhibition of gastric acid secretion, treatment of a gastrointestinal disorder and treatment of an airway disorder.

Applicants submit that in view of the claim amendments and arguments presented herein, the rejection of claims 29, 31, 32, 36, and 38 under 35 U.S.C. § 112, first paragraph, is improper and should be withdrawn.

II. Rejection under 35 U.S.C. §103(a)

Claims 1, 2, 15-17, 27-29, 31, 32, 35, 36, and 38 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over each of the following four documents:

WO 2003/094967 to Hanauer et al. ("Hanauer");

WO 2002/064118 to Juppo et al. ("Juppo");

WO 2002/020523 to Elman et al. ("Elman"); and

WO 1999/055706 to Amin et al. ("Amin").

The Examiner alleges that each of the four documents discloses the instant compound, pharmaceutical composition, and method of using the compound. The Examiner acknowledges, however, that each of the cited documents does not disclose the specific claimed mesylate salt, but alleges that one of ordinary skill in the art would have been motivated to modify the disclosed compound to obtain the instant claimed mesylate salt. The Examiner also alleges that changing one salt to another is within the skill of the artisan and that mesylate is a common salt.

Applicants disagree with the Examiner's allegations. Although these publications may disclose the compound 2,3-dimethyl-8-(2,6-dimethylbenzylamino)-N-hydroxyethyl-imidazo-[1,2-a]pyridine-6-carboxamide in a neutral form, none of these documents discloses Applicants' claimed mesylate salt. There is also no suggestion in any of these documents that the Applicants' particular mesylate salt would have any particular or advantageous properties.

A. The claimed compounds have higher bioavailability and faster absorption than the corresponding HCl salt or the free base.

Unexpectedly, the claimed mesylate salt has superior properties compared to the compound in the form of a free base or an HCl salt. In this regard, Applicants have conducted biological tests demonstrating that the mesylate salt has higher bioavailability and faster absorption than the free base or the HCl salt. At the Examiner's request, Applicants will submit the data presented herein in the form of a declaration.

Dissolution experiments and a dog study were performed in order to evaluate the performance of different forms of the active compound. *In vitro* dissolution experiments were performed and two immediate release formulations, one containing the mesylate salt and the other containing the HCl salt, were tested in fasted pH modified dogs.

All tablets contained either the HCl salt or mesylate salt of the active compound with the dose being 75 mg. The following immediate release ("IR") formulations were used in the study:

TR12205: IR formulation containing the HCl salt; and

TR11281: IR formulation containing the mesylate salt

1. In vitro results:

The dissolution rates of the two salts were evaluated using the rotating disc method. The results show that the dissolution rate in human intestinal fluid was several folds higher for the mesylate salt compared to the HCl salt or the free form (see Figure 1). This difference indicates that the mesylate salt will have a higher bioavailability and faster absorption *in vivo*.

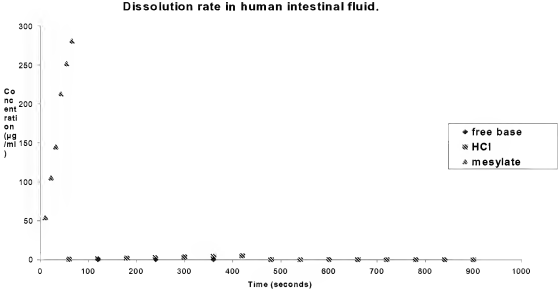

Figure 1- Dissolution rate of compound in human intestinal fluid using the rotating disc method.

In contrast, the two tablet formulations TR12205 (HCl salt) and TR11281 (mesylate salt) had similar *in vitro* dissolution profiles in citrate buffer at pH 4. The dissolution rate was slightly slower for the formulation containing the HCl salt formulation in the citrate buffer method, as shown in Fig. 2.

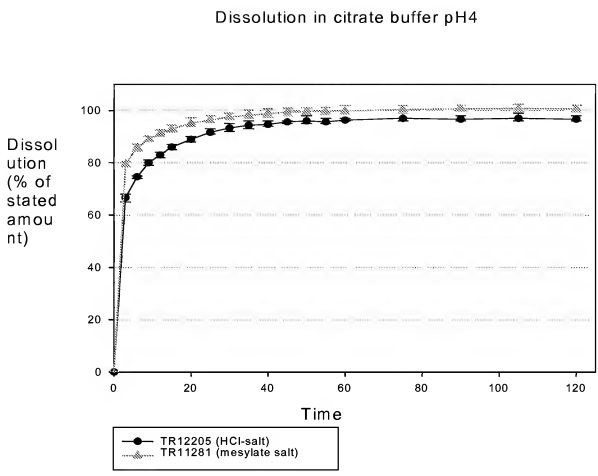

Figure 2-Average dissolution profiles of TR12205 (HCl salt) and TR11281 (mesylate salt) in citric buffer pH 4.

2. In vivo results:

Tablets containing the mesylate salt were administered p.o to fasted dogs with reduced gastric pH (pH 1) and elevated gastric pH (pH 6) prior to tablet dosing. Tablets containing the HCl salt were administered to dogs having elevated gastric pH (pH 6).

Significant differences were detected for both the response variables AUC and Cmax. The mesylate salt formulation both at pH 1 and at pH 6 was better than the HCl salt formulation at pH 6 (See Figure 3).

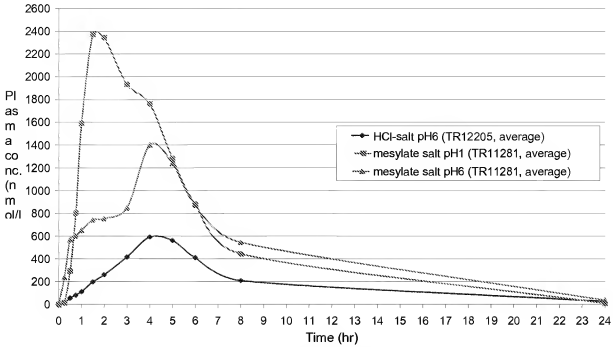

Figure 3-Average plasma profiles after p.o administration of IR formulations containing 75 mg of active compound to fasted pH modified dogs.

The *in vitro* dissolution data from the rotating disc method discriminated well for the differences shown in exposure *in vivo*. The dissolution data in citrate buffer pH 4 are less suitable to indicate how the salts perform *in vivo*.

From these results, it can be concluded that using the mesylate salt is unexpectedly superior in comparison to the HCl salt in the immediate release formulations because it has both a higher bioavailability and faster absorption.

The above biological test data demonstrates that the claimed mesylate salt has superior pharmacological properties compared to the free base and to the hydrochloride salt. These properties would not have been predictable to one of ordinary skill in the art in view of Hanauer, Juppo, Elman, or Amin. Therefore, the pending claims are nonobvious.

Withdrawal of the rejection of claims 1, 2, 15-17, 27-29, 31, 32, 35, 36, and 38 under 35 U.S.C. §103(a) is respectfully requested.

III. Conclusion

Upon entry of this Amendment, claims 1-24, 27-29, 32, 35, 36, and 38 remain pending. Applicants respectfully submit that the pending claims are directed to patentable subject matter. Accordingly, Applicants request expedited allowance of the instant application. No new matter has been added by any amendment herein.

Authorization is hereby given to charge any fee in connection with this communication to Deposit Account No. 23-1703.

Dated: January 10, 2008

Respectfully submitted,

/Andrew Fessak/
Reg. No. 48,528
Customer No. 07470
Direct Line: (212) 819-8437